

Title (en)

METHOD FOR PRODUCING ANTI-HER3 ANTIBODY-DRUG CONJUGATE

Title (de)

VERFAHREN ZUR HERSTELLUNG VON ANTI-HER3-ANTIKÖRPER-ARZNEIMITTEL-KONJUGAT

Title (fr)

PROCÉDÉ DE PRODUCTION DE CONJUGUÉ ANTICORPS-MÉDICAMENT ANTI-HER3

Publication

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Application

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Priority

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Abstract (en)

Provided is a method for producing an antibody-drug conjugate comprising reacting a compound represented by the following formula:  $(\text{maleimid-N-yl})-(\text{CH<sub>n</sub>}-\text{L<sub>n</sub>}-\text{C}(\text{=O})-\text{L<sub>n</sub>}-\text{P<sub>n</sub>}-\text{NH}-(\text{CH<sub>n</sub>}-\text{L<sub>n</sub>}-\text{C}(\text{=O})-\text{L<sub>n</sub>}-\text{P<sub>n</sub>}-\text{NH-DX})$  or  $(\text{maleimid-N-yl})-(\text{CH<sub>n</sub>}-\text{L<sub>n</sub>}-\text{C}(\text{=O})-\text{L<sub>n</sub>}-\text{P<sub>n</sub>}-\text{NH-DX})$  with an anti-HER3 antibody or a reactive derivative thereof, thus conjugating a drug-linker moiety to the antibody, by forming a thioether bond on a disulfide bond moiety present in a hinge part of the antibody, wherein -(NH-DX) represents a group represented by the following formula: wherein the nitrogen atom of the amino group at position 1 is the connecting position.

IPC 8 full level

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CPC (source: CN EP IL KR RU US)

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Citation (applicant)

- JP H0559061 A 19930309 - DAIICHI SEIYAKU CO [JP], et al
- JP H08337584 A 19961224 - DAIICHI SEIYAKU CO, et al
- WO 9746260 A1 19971211 - DAIICHI SEIYAKU CO [JP], et al
- WO 0025825 A1 200000511 - DAIICHI SEIYAKU CO [JP], et al
- US 5968511 A 19991019 - AKITA ROBERT [US], et al
- US 5480968 A 19960102 - KRAUS MATTHIAS H [US], et al
- WO 03013602 A1 20030220 - MAX PLANCK GESELLSCHAFT [DE], et al
- WO 2007077028 A2 20070712 - U3 PHARMA AG [DE], et al
- WO 2008100624 A2 20080821 - MERRIMACK PHARMACEUTICALS INC [US], et al
- WO 2012019024 A2 20120209 - IMMUNOGEN INC [US], et al
- WO 9007861 A1 19900726 - PROTEIN DESIGN LABS INC [US]
- WO 9201047 A1 19920123 - CAMBRIDGE ANTIBODY TECH [GB], et al
- WO 9220791 A1 19921126 - CMABRIDGE ANTIBODY TECH [GB], et al
- WO 9306213 A1 19930401 - MEDICAL RES COUNCIL [GB], et al
- WO 9311236 A1 19930610 - MEDICAL RES COUNCIL [GB], et al
- WO 9319172 A1 19930930 - CAMBRIDGE ANTIBODY TECH [GB], et al
- WO 9501438 A1 19950112 - MEDICAL RES COUNCIL [GB], et al
- WO 9515388 A1 19950608 - MEDICAL RES COUNCIL [GB], et al
- WO 9954342 A1 19991028 - UMANA PABLO [CH], et al
- WO 0061739 A1 200001019 - KYOWA HAKKO KOGYO KK [JP], et al
- WO 0231140 A1 20020418 - KYOWA HAKKO KOGYO KK [JP]
- US 4816397 A 19890328 - BOSS MICHAEL A [GB], et al
- US 5916771 A 19990629 - HORI NOBUAKI [JP], et al
- US 6207418 B1 20010327 - HORI NOBUAKI [JP], et al
- US 6207418 B1 20010327 - HORI NOBUAKI [JP], et al
- JP H0687746 A 19940329 - DAIICHI SEIYAKU CO, et al
- JP 2002060351 A 20020226 - DAIICHI SEIYAKU CO
- WO 03038043 A2 20030508 - UAB RESEARCH FOUNDATION [US], et al
- DUCRY, L. ET AL., BIOCONJUGATE CHEM, vol. 21, 2010, pages 5 - 13
- ALLEY, S. C. ET AL., CURRENT OPINION IN CHEMICAL BIOLOGY, vol. 14, 2010, pages 529 - 537
- DAMLE N.K., EXPERT OPIN. BIOL. THER., vol. 4, 2004, pages 1445 - 1452
- SEENTER P. D. ET AL., NATURE BIOTECHNOLOGY, vol. 30, 2012, pages 631 - 637
- KUMAZAWA, E.TOHGO, A., EXP. OPIN. INVEST. DRUGS, vol. 7, 1998, pages 625 - 632
- IMITSUI, I. ET AL., JPN J. CANCER RES., vol. 86, 1995, pages 776 - 786

- TAKIGUCHI, S. ET AL., JPN J. CANCER RES., vol. 88, 1997, pages 760 - 769
- JOTO, N. ET AL., INT J. CANCER, vol. 72, 1997, pages 680 - 686
- KUMAZAWA, E. ET AL., CANCER CHEMOTHER. PHARMACOL., vol. 42, 1998, pages 210 - 220
- DE JAGER, R. ET AL., ANN N Y ACAD SCI, vol. 922, 2000, pages 260 - 273
- INOUE, K. ET AL.: "Polymer Drugs in the Clinical Stage", 2003, pages: 145 - 153
- KUMAZAWA, E. ET AL., CANCER SCI, vol. 95, 2004, pages 168 - 175
- SOEPENBERG, O. ET AL., CLINICAL CANCER RESEARCH, vol. 11, 2005, pages 703 - 711
- WENTE M. N. ET AL., INVESTIGATIONAL NEW DRUGS, vol. 23, 2005, pages 339 - 347
- PLOWMAN ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 87, 1990, pages 4905 - 4909
- KRAUS ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 86, 1989, pages 9193 - 9197
- HOLLINGER ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 90, 1993, pages 6444 - 6448
- ALIMANDI ET AL., ONCOGENE, vol. 10, 1995, pages 1813 - 1821
- DEFAZIO ET AL., INT. J. CANCER, vol. 87, 2000, pages 487 - 498
- NADIU ET AL., BR. J. CANCER, vol. 78, 1998, pages 1385 - 1390
- SKERRA, J. MOL. RECOG., 2000
- JONES ET AL., NATURE, vol. 321, 1986, pages 522 - 525
- RIECHMANN ET AL., NATURE, vol. 332, 1988, pages 323 - 329
- PRESTA, CURR. OP. STRUCT. BIOL., vol. 2, 1992, pages 593 - 596
- MORRISON ET AL., PROC. NATL. ACAD. SCI. U.S.A., vol. 81, 1984, pages 6851 - 6855
- TOMIZUKA, K. ET AL., NATURE GENETICS, vol. 16, 1997, pages 133 - 143
- KUROIWA, Y. ET AL., NUCL. ACIDS RES., vol. 26, 1998, pages 3447 - 3448
- YOSHIDA, H. ET AL.: "Animal Cell Technology: Basic and Applied Aspects", vol. 10, 1999, KLUWER ACADEMIC PUBLISHERS, pages: 69 - 73
- TOMIZUKA, K. ET AL., PROC. NATL. ACAD. SCI. USA, vol. 97, 2000, pages 722 - 727
- ANNU. REV. IMMUNOL., vol. 113, 1994, pages 433 - 455
- MUYDERMANS ET AL., REVIEWS IN MOLECULAR BIOTECHNOLOGY, vol. 74, pages 277 - 302
- HOLT ET AL., TRENDS BIOTECHNOL., vol. 21, pages 484 - 90
- CELL DEATH AND DIFFERENTIATION, vol. 15, 2008, pages 751 - 761
- MOLECULAR BIOLOGY OF THE CELL, vol. 15, December 2004 (2004-12-01), pages 5268 - 5282
- BIO TECHNIQUES, vol. 28, January 2000 (2000-01-01), pages 162 - 165
- KOHLERMILSTEIN, NATURE, vol. 256, 1975, pages 495 - 497
- URLAUB, G.CHASIN, L. A., PROC. NATL. ACAD. SCI. USA, vol. 77, 1980, pages 4126 - 4220
- SAIKI, R. K. ET AL., SCIENCE, vol. 239, 1988, pages 487 - 489
- GLUZMAN, Y., CELL, vol. 23, 1981, pages 175 - 182
- WEIR, D. M.: "Handbook of Experimental Immunology", vol. 1, 2, 3, 1978, BLACKWELL SCIENTIFIC PUBLICATIONS
- KABAT, E. A.MAYER, M. M.: "Experimental Immunochemistry", 1964, CHARLES C THOMAS PUBLISHER
- KOHLER ET AL., EUR. J. IMMUNOL., vol. 6, 1977, pages 511
- MILSTEIN ET AL., NATURE, vol. 266, 1977, pages 495
- PROC. NATL. ACAD. SCI. USA, vol. 81, 1984, pages 6851 - 6855
- BOWIE ET AL., SCIENCE, vol. 253, 1991, pages 164
- WORMSTONE, I. M. ET AL., INVESTIGATIVE OPHTHALMOLOGY & VISUAL SCIENCE, vol. 43, no. 7, 2002, pages 2301 - 2308
- CARMEN, S. ET AL., BRIEFINGS IN FUNCTIONAL GENOMICS AND PROTEOMICS, vol. 1, no. 2, 2002, pages 189 - 203
- SIRIWARDENA, D. ET AL., OPHTHALMOLOGY, vol. 109, no. 3, 2002, pages 427 - 431
- NATURE BIOTECHNOLOGY, vol. 23, no. 9, 2005, pages 1105 - 1116
- "Proteins, Structures and Molecular Principles", 1984, W. H. FREEMAN AND COMPANY
- THORNTON, NATURE, vol. 354, 1991, pages 105
- ALTSCHUL, STEPHEN F.THOMAS L. MADDENALEJANDRO A. SCHAEFFERJINGHUI ZHANGZHENG ZHANGWEBB MILLERDAVID J. LIPMAN: "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs", NUCLEIC ACIDS RES., vol. 25, 1997, pages 3389 - 3402, XP002905950, DOI: 10.1093/nar/25.17.3389
- LORI BURTON, PHARMACEUTICAL DEVELOPMENT AND TECHNOLOGY, vol. 12, 2007, pages 265 - 273
- JOURNAL OF CHROMATOGRAPHY A, vol. 705, 1995, pages 129 - 134
- ANALYTICAL BIOCHEMISTRY, vol. 360, 2007, pages 75 - 83
- IDUSOGIE ET AL., J IMMUNOL., vol. 166, pages 2571 - 2575
- SHIELDS ET AL., J BIOL CHEM., vol. 276, pages 6591 - 6604
- "A Laboratory Course Manual", 1996, COLD SPRING HARBOR LABORATORY PRESS, article "Strategies for Protein Purification and Characterization"
- "Antibodies: A Laboratory Manual", 1988, COLD SPRING HARBOR LABORATORY
- HERMANSON, G.T: "Bioconjugate Techniques", 1996, ACADEMIC PRESS, pages: 56 - 136,456-493
- PROTEIN SCIENCE, vol. 4, 1995, pages 2411 - 2423
- J. ORG. CHEM., vol. 51, 1986, pages 3196

#### Citation (search report)

- [AD] WO 2012019024 A2 20120209 - IMMUNOGEN INC [US], et al
- [A] WO 2012064733 A2 20120518 - MEDIMMUNE LLC [US], et al
- [YP] WO 2014057687 A1 20140417 - DAIICHI SANKYO CO LTD [JP]
- [YP] WO 2014061277 A1 20140424 - DAIICHI SANKYO CO LTD [JP]

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AU 2020200227 B2 20211007; AU 2021286320 A1 20220120; AU 2021286320 B2 20240418; BR 112016017893 A2 20171017;  
BR 112016017893 B1 20220823; CA 2939802 A1 20151015; CA 2939802 C 20221101; CN 106163559 A 20161123; CN 106163559 B 20200218;  
CN 111228511 A 20200605; CN 111228511 B 20240618; CY 1124071 T1 20220527; DK 3129063 T3 20210406; EP 3129063 A1 20170215;  
EP 3129063 B1 20210127; EP 3789042 A1 20210310; ES 2859648 T3 20211004; HR P20210593 T1 20210514; HU E054411 T2 20210928;  
IL 248239 A0 20161130; IL 248239 B 20220701; IL 293177 A 20220701; IL 293177 B1 20230301; IL 293177 B2 20230701;  
IL 300540 A 20230401; IL 300540 B1 20240401; IL 311108 A 20240401; JP 2017197515 A 20171102; JP 2017222638 A 20171221;  
JP 2017503784 A 20170202; JP 2019135248 A 20190815; JP 2020143114 A 20200910; JP 2021169515 A 20211028;  
JP 2022180416 A 20221206; JP 2024019172 A 20240208; JP 6105171 B2 20170329; JP 6148422 B1 20170614; JP 6513128 B2 20190515;  
JP 6707696 B2 20200610; JP 6918182 B2 20210811; JP 7138750 B2 20220916; JP 7383772 B2 20231120; KR 101937549 B1 20190110;  
KR 102127623 B1 20200629; KR 102186027 B1 20201203; KR 102239413 B1 20210412; KR 102351755 B1 20220114;  
KR 102399277 B1 20220518; KR 102445502 B1 20220921; KR 102495426 B1 20230206; KR 102624244 B1 20240111;  
KR 20160144396 A 20161216; KR 20190004837 A 20190114; KR 20200077620 A 20200630; KR 20200136052 A 20201204;

KR 20210041126 A 20210414; KR 20210115056 A 20210924; KR 20220012402 A 20220203; KR 20220068270 A 20220525;  
KR 20220132025 A 20220929; KR 20230021173 A 20230213; KR 20240008415 A 20240118; LT 3129063 T 20210625;  
MX 2016010533 A 20161212; MX 2021004884 A 20210615; MY 195180 A 20230111; NZ 722668 A 20240223; PH 12016501711 A1 20161219;  
PL 3129063 T3 20210712; PT 3129063 T 20210401; RS 61711 B1 20210531; RU 2016143351 A 20180515; RU 2016143351 A3 20190305;  
RU 2019143766 A 20200220; RU 2711640 C2 20200117; SG 10201907807X A 20190927; SG 11201608309P A 20161129;  
SI 3129063 T1 20210831; TW 201542230 A 20151116; TW 202108176 A 20210301; TW 202218685 A 20220516; TW I704928 B 20200921;  
TW I745021 B 20211101; TW I826828 B 20231221; US 10383878 B2 20190820; US 11298359 B2 20220412; US 2017021031 A1 20170126;  
US 2019151328 A1 20190523

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**JP 2015002020 W 20150410;** AU 2015245122 A 20150410; AU 2020200227 A 20200113; AU 2021286320 A 20211215;  
BR 112016017893 A 20150410; CA 2939802 A 20150410; CN 201580019138 A 20150410; CN 202010034933 A 20150410;  
CY 211100356 T 20210426; DK 15719011 T 20150410; EP 15719011 A 20150410; EP 20200710 A 20150410; ES 15719011 T 20150410;  
HR P20210593 T 20210413; HU E15719011 A 20150410; IL 24823916 A 20161006; IL 29317722 A 20220519; IL 30054023 A 20230209;  
IL 31110824 A 20240226; JP 2016540705 A 20150410; JP 2017037872 A 20170301; JP 2017098589 A 20170518; JP 2019073941 A 20190409;  
JP 2020087844 A 20200520; JP 2021119487 A 20210720; JP 2022141262 A 20220906; JP 2023190804 A 20231108;  
KR 20167029685 A 20150410; KR 20197000169 A 20150410; KR 20207018066 A 20150410; KR 20207033997 A 20150410;  
KR 20217010205 A 20150410; KR 20217028736 A 20150410; KR 20227001001 A 20150410; KR 20227016151 A 20150410;  
KR 20227031970 A 20150410; KR 20237003389 A 20150410; KR 20247000775 A 20150410; LT 15719011 T 20150410;  
MX 2016010533 A 20150410; MX 2021004884 A 20160812; MY PI2016001655 A 20150410; NZ 72266815 A 20150410;  
PH 12016501711 A 20160830; PL 15719011 T 20150410; PT 15719011 T 20150410; RS P20210435 A 20150410; RU 2016143351 A 20150410;  
RU 2019143766 A 20150410; SG 10201907807X A 20150410; SG 11201608309P A 20150410; SI 201531545 T 20150410;  
TW 104111534 A 20150410; TW 109127496 A 20150410; TW 110135505 A 20150410; US 201615285156 A 20161004;  
US 201916264395 A 20190131